Aerosol dispersion in a ventilator circuit: towards a model for enhancing our understanding of ventilator-associated pneumonia

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Abstract

Background
Patients receiving mechanical ventilation for more than 48 hours are at risk for developing ventilator-associated pneumonia (VAP).
Methods
We investigated aerosol flow in a ventilator circuit attached to test lungs to better understand how airflow dynamics in ventilator tubing can contribute to the pathogenesis of VAP. The ventilator was operated so that the lungs cyclically inflated and deflated. Aerosolized saline was used as a surrogate for bioaerosols and was generated in the circuit with an aerosol generator attached to the tubing below an endotracheal cuff that sealed an endotracheal tube at the opening of the lungs. We used a particle collector and analyzer attached to the circuit approximately two feet from the opening of the lungs to determine whether aerosols flowed into the tubing.
Results
We detected significant levels of aerosolized particles ($P < 0.05$) that traveled retrogradely into the ventilator circuit. The highest nozzle pressure tested, 13 hPa, produced mean 0.5, 0.7 and 1.0 μm aerosol levels of 24 ±5, 10±4 and 8±3 particles/ft ^{3}, respectively. The lowest nozzle pressure tested, 10 hPa, produced mean 0.5, 0.7 and 1.0 μm aerosol levels of 14 ±5, 4 ±2, and 3 ±2 particles/ft3.
Conclusions
Aerosolized material that enters the circuit near the endotracheal cuff travels into the ventilator tubing during mechanical ventilation. Our results suggest that infectious material could travel a similar route and contaminate the air in the ventilator circuit which then enters the patient.

Keywords: ventilator-associated pneumonia, bioaerosol, aerosol, contamination, ventilator circuit

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Introduction

It has been estimated that over 300,000 patients receive mechanical ventilation in the US each year. [1-3] The average number of days a patient receives ventilation varies with patient type. One study that investigated 42 intensive care units at 40 different hospitals reported average durations between 2.9 and 7.9 days with patient characteristics heavily influencing the outcome. [4] Note that much longer ventilation times can occur. Mechanical ventilation can cause various complications, referred to as ventilator-associated events, including ventilator associated pneumonia (VAP), which is a lung infection that occurs in patients receiving invasive mechanical ventilation and caused by infectious agents not incubating or present at the time ventilation started. [5] Reports have indicated that the incidence of developing VAP ranges from 5-40% depending on various factors including the setting and conditions of the patients. [6-8] VAP typically occurs after the first 48 hours of mechanical ventilation and has significant burdens on patient well-being and economic costs. The reported mortality of VAP typically ranges from 10-50%, and in some settings has been reported to be as high as 76%. [9,10] Prolonged mechanical ventilation times and ICU stays are unfavorable outcomes strongly associated with the development of VAP. Increased healthcare costs resulting from VAP are estimated to be over $40,000 per incidence. [11]

Pneumonia, the eighth leading cause of death in the United States in 2017 combined with influenza,[12] is a lower respiratory tract infection that causes inflammation and fluid build-up in the pulmonary parenchyma. Micro-aspiration of colonies on the surfaces of the oropharyngeal airways appears to be the most common pathway by which pathogens enter the lungs and cause infection. While the respiratory tract contains a number of defenses to protect the lungs, [5] intubation compromises the natural barrier between the oropharynx and trachea. Fluid build-up at the endotracheal tube cuff provides a pooling area for pathogens to reside and opportunistically pass through the pneumatic seal. [13,14] As fluid gradually seeps through the cuff-trachea interface, access is granted to the lungs. Aerosolized material via aspiration and coughing gives access to the ventilator circuit. Once in the circuit as an aerosol, pathogens gain the possibility to re-enter the patient as an airborne pathogen, which is expected to facilitate entry to the lungs and ultimately infection. Several studies have indicated that ventilator systems become contaminated with various bacteria upon use. [15-18] The growth of colony forming units on the walls of the tubes can lead to bioaerosol formation over time given the constant cyclic flow of air which can disperse surface-laden micro-organisms into the confined circuit volume that ultimately leads to the lungs. Via the pathway described above, pathogens can enter the ventilator circuit after first collecting in oral and nasopharyngeal secretions. Gaining a better understanding of the dynamics of aerosol dispersion in ventilator circuits will help elucidate the full mechanistic pathway by which infection occurs and hence provide insights that can lead to better prophylaxis. For example, understanding whether significant quantities of aerosols originating below the endotracheal tube cuff can reach the ventilator tube will guide the development of new strategies for protecting the patient airway.

Several studies have utilized non-biological aerosols as a safe surrogate to better understand bioaerosol behavior. For example, saline has been used as a surrogate for bioaerosols produced during aerosol generating procedures and allowed for safe testing of a medical device in clinical and experimental environments. [19,20] Additional studies have used various nonviable particles as safe alternatives to bioaerosols. [21-23] A comparison between nonbiological aerosols containing either oleic acid or KCl and biological aerosols consisting of gram positive bacteria, molds or MS2 bacteriophage found good agreement in testing the filtration efficiency of a room air cleaner. [24] Applying aerosol studies to mechanical ventilation will help in better understanding the potential for aerosol diffusion into the circuit, which will help in developing new technologies that can potentially reduce the occurrence of VAP.

In this study, we examine the flow pattern of saline aerosols in a ventilator circuit. Using a polydisperse aerosol generator, saline aerosols are injected into a closed ventilator-test lung circuit in the vicinity of aspiration (where the endotracheal tube cuff seals against the trachea just above the lungs) and collected and analyzed at a distal port connected to a particle collector (Figure 1). We show that aerosols flow freely up the endotracheal tube and into the ventilator tubing while the ventilator undergoes cyclic inflation and deflation of the test lungs. The system represents a useful model for studying contamination of ventilator circuits during mechanical ventilation and demonstrates aerosol motility throughout the ventilation circuit.

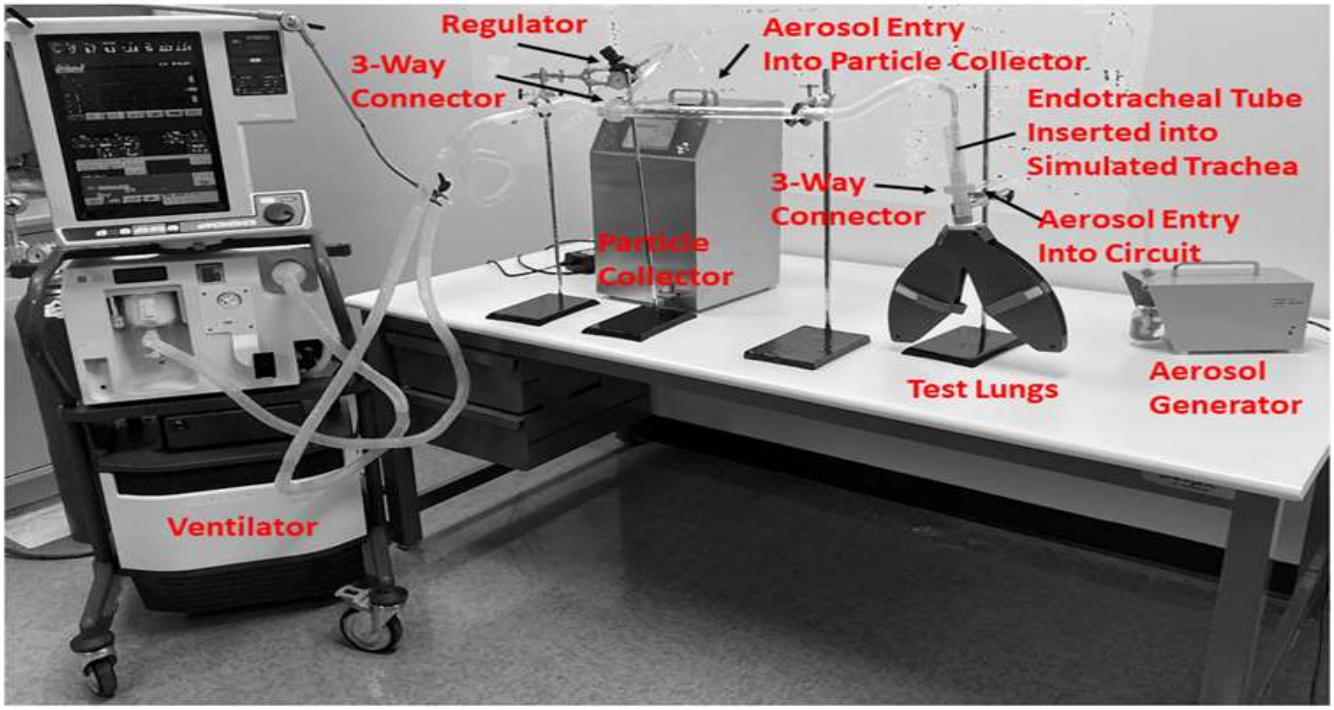

Figure 1: The experimental setup consists of a closed circuit connecting the ventilator to test lungs with ports for aerosol entry and particle collection

Methods

The experimental setup is shown in Figure 1. Due to the inherent difficulties of using infectious materials, saline aerosols were used as a surrogate for bioaerosols. An 80 ml saline solution (0.9% NaCl in H_2O) was added to a glass vial containing a screw top opening and attached to a polydisperse aerosol generator (TSI, Minneapolis, MN). Aerosols were generated for 10 s at nozzle pressures of 10, 11, 12 and 13 hPa. A BioTrak Real-Time Viable Particle Counter (TSI, Minneapolis, MN) was used to detect and determine the concentration and size distribution of aerosols. Mechanical ventilation of test lungs was performed using a Puritan Bennet 840 mechanical ventilator and TL2 Pro elastic test lungs (South Pacific Biomedical) that had a volume of 2.0 l. The ventilator supplied a mixture of compressed air, supplied by a Puritan Bennet air compressor, and oxygen from a standard cylinder (Air Gas) containing a regulator set at approximately 40 PSI. The breath delivery unit was operated in VC mode with a passive lung model using the following settings: tidal volume (V_T – 500 mL); peak inspiratory flow (VMAX) of 44 l/min; FiO_2: 21%; positive end expiratory pressure (PEEP) of 3.0 cm H_2O; plateau time (TPL) of 0.0s; respiratory rate (f) of 10 /min. A 3D printed three-way connector was used to attach the ventilator tube to the particle collector. The particle collector was attached to the connector using Tygon tubing. A regulator was inserted into the connection between the particle collector and ventilator tube. The regulator was open to the minimum amount that allowed the ventilator to run with an open connection to the particle collector, allowing air to flow freely and uninterrupted to the particle collector and test lungs during aerosol exposure and particle collection. Without the regulator, significant loss of pressure was observed. A plastic tube was used to attach the ventilator tube at the three-way connection to additional flexible tubing attached to an endotracheal tube that was inserted into a 10 cm plastic tube that served as a simulated trachea. The endotracheal tube cuff was inflated with a syringe to seal the endotracheal tube within the simulated trachea. A second three-way connector was attached to the bottom of the simulated tracheobronchial junction. One of the two other ports on this connector was attached to the elastic test lungs that could be inflated and deflated in response to mechanical ventilation. The second port was attached to a polydisperse aerosol generator using Tygon tubing. During testing, the system remained sealed at the aerosol generator.

Background aerosol levels were initially analyzed with the ventilator running without aerosolization (control group). The particle collector was run for 30 s with a 30 s initial delay. For experimental conditions of 10, 11, 12 and 13 hPa, aerosol generation was performed for 10 s during the final 10 s of delay prior to particle collection. Hence, immediately upon stopping aerosol generation, particle collection was started and lasted for 30 s. 25 runs were performed for each condition. Experimental values were compared with controls. Data were compared with descriptive statistics (mean, standard deviation, median, interquartile range) and with Student's t-test. $P<0.05$ was considered statistically significant.

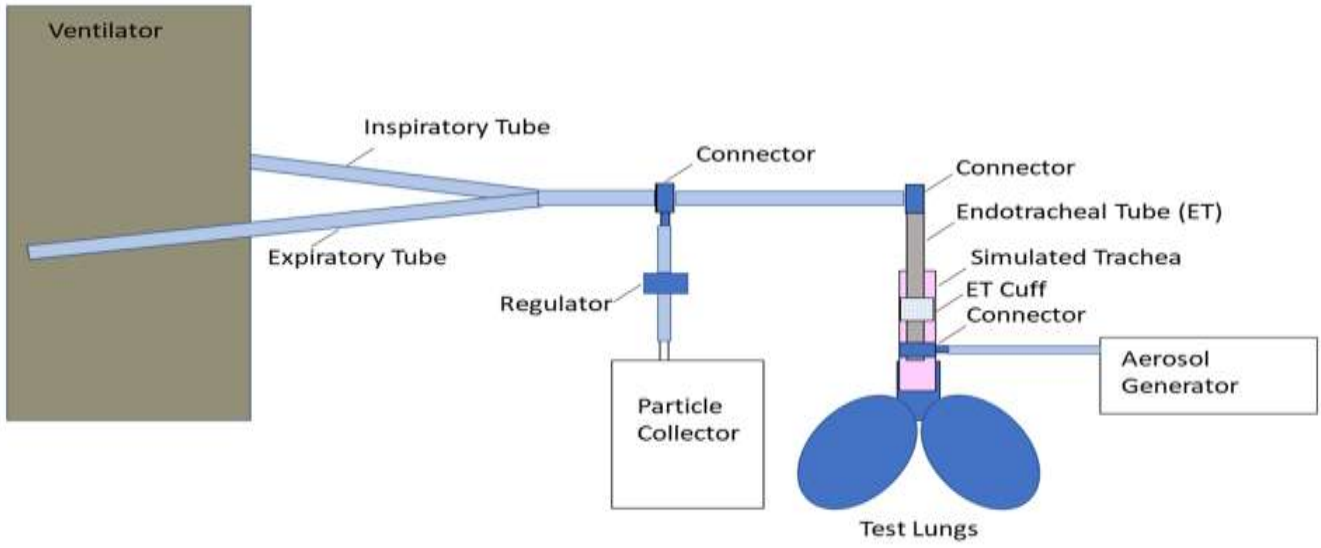

Figure 2: Diagram of experimental set-up

Results

Mean and median 0.5, 0.7 and 1.0 μm particle levels (particles/ft^3) for all experiments are summarized in Table 1. For the control group, which sampled air in the ventilator tube without the injection of saline aerosols, the mean concentrations of particles detected in the ventilator tubing while ventilating test lungs for 0.5, 0.7 and 1.0 μm particles were, respectively, 11 ±3, 2 ±2, and 1 ±1 particles/ft^3. For the experimental group, saline aerosols were injected for 10 s into the system where the bottom of the endotracheal tube is near the opening of the test lungs. The ventilator was constantly ventilating the test lungs before, during and after aerosol injection. When the aerosol generator nozzle pressure was set at 10 hPa, the mean concentrations of 0.5, 0.7 and 1.0 μm particles that reached the detector were, respectively, 14 ±5, 4 ±2, and 3 ±2 particles/ft^3. The P-values for the 0.5, 0.7, and 1.0 μm particles concentrations compared to the control are, respectively, 0.002, < 0.001, and < 0.001.

When the aerosol nozzle pressure was set at 11 hPa, the mean concentrations of 0.5, 0.7 and 1.0 μm particles that reached the detector were, respectively, 14 ±4, 5 ±2, and 4 ±2 particles/ft^3. The P-values for the 0.5, 0.7, and 1.0 μm particles concentrations compared to the control are, respectively, < 0.001, < 0.001, and < 0.001.

When the aerosol nozzle pressure was set at 12 hPa, the mean concentrations of 0.5, 0.7 and 1.0 μm particles that reached the detector were, respectively, 17 ±6, 6 ±3 and 5 ±2 particles/ft^3. The P-values for the 0.5, 0.7, and 1.0 μm particles concentrations compared to the control are, respectively, < 0.001, < 0.001, and < 0.001.

When the aerosol nozzle pressure was set at 13 hPa, the mean concentrations of 0.5, 0.7 and 1.0 μm particles that reached the detector were, respectively, 24 ±5, 10 ±4, and 8 ±3 particles/ft^3.

The P-values for the 0.5, 0.7, and 1.0 μm particles concentrations compared to the control are, respectively, < 0.001, < 0.001, and <0.001.

Nozzle Pressure	Control			10 hPa			11 hPa			12 hPa			13 hPa		
Particle Size (mm)	0.5	0.7	1.0	0.5	0.7	1.0	0.5	0.7	1.0	0.5	0.7	1.0	0.5	0.7	1.0
Mean (particles/ ft.^{3})	11	2	1	14	4	3	14	5	4	17	6	5	24	10	8
SD	3	2	1	5	2	2	4	2	2	6	3	2	5	4	3
Median (particles/ ft.^{3})	11	2	1	14	5	3	14	5	4	16	6	5	23	10	8
Q1	8	1	1	12	3	2	11	3	3	11	4	4	21	6	6
Q3	13	3	3	16	6	4	16	6	5	20	7	7	26	13	10
IQR	5	2	2	4	3	2	5	3	2	9	3	3	5	7	4

Table 1: Mean, standard deviation (SD), median and interquartile range (IQR) for all particle sizes 0.5, 0.7 and 1.0 mm aerosolized at nozzle pressures of 10, 11, 12, and 13 hPa are shown

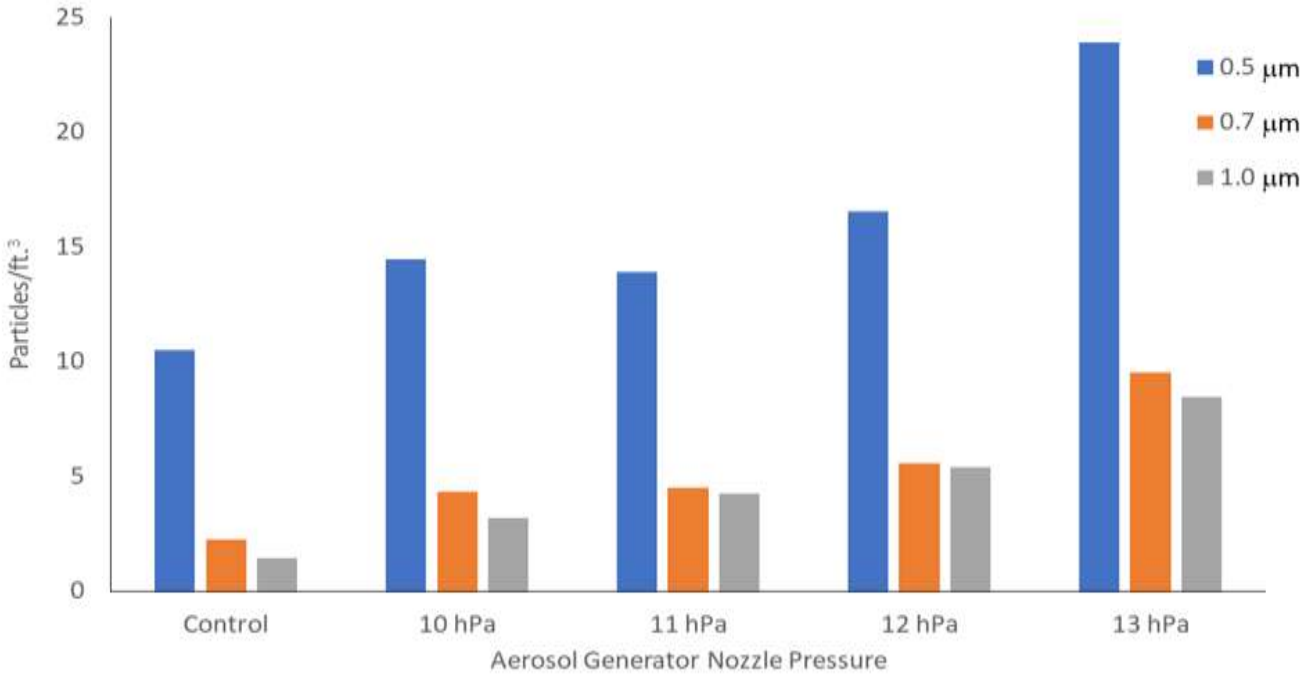

Figure 3: A bar graph comparing particle concentration data for sizes 0.5, 0.7 and 1.0 mm generated at nozzle pressures of 10, 11, 12 and 13 hPa is shown

Discussion

This study demonstrates that aerosols generated below the sealed endotracheal cuff in a closed and mechanically ventilated circuit can travel into the ventilator tubes. The aerosols were found to disperse in a retrograde fashion into the ventilator tubing. In our set-up, aerosols traveled through more than two feet of tubing in the direction opposite the lungs. The amount of aerosol generated is proportional to the nozzle pressure on the aerosol generator. In all cases, significant quantities of aerosol were detected at the particle collector in the size range of 0.5-1.0 µm, which is comparable to the length scales of bacteria and viruses. We tested

relatively low nozzle pressures in order to see if detectable aerosol migration occurred when minimal levels of aerosols were generated. Our selected range is comparable to typical average circuit pressures of 6-7 hPa for an entire breath cycle without aerosolization in our setup and typical maximum pressures of 14-17 hPa measured during the inspiratory phase. Low levels of aerosol production might be relevant to a condition in which small amounts of fluid in the trachea leaks below the endotracheal cuff. Coughing would be expected to give much higher quantities of aerosols, which would more easily disperse into the ventilator tube. Further experiments with bacterial and/or viral bioaerosols will need to be performed.

The detection of aerosols in air sampled in the ventilator tube shows that aerosols in a size range comparable to microbes can travel outside the patient's airway. Aerosols do not simply settle into the lungs upon generation. They can travel into the ventilator tubing and potentially contaminate the surface and form biofilms. Bacterial contamination of ventilator tubing has been reported. [25] During the mechanical ventilation cycle, airflow is directed both towards and away from the patient's airway at different times, facilitating aerosol travel in both directions. Aerosolized pathogens could re-enter the intubated patient and migrate directly into the lungs. Depending on the rate of aerosol production, a constant flux of bioaerosols into and out of the patient might be realized.

Note that the aerosol generator tubing is not connected directly to the endotracheal tube. The aerosolized material can travel either into the lungs or travel retrogradely into the endotracheal tube. It is likely that some quantity of aerosols diffuse downward into the lungs, however, once in the lungs there is no barrier that would prevent movement upwards and into the endotracheal tube. The cyclical deflation of the lungs is expected to facilitate upward diffusion. Regardless of the exact path, aerosols can migrate upwards and into the ventilator tubes which are outside of the patient. The extent of this migration in the closed circuit suggests that patients can be re-exposed to potentially infectious material during the timeframe of mechanical ventilation. Exposure to pathogens that enter the ventilator tubing can potentially be more dangerous than pathogens that settle in fluid at the endotracheal cuff because airborne pathogens might more deeply penetrate the lung and circumvent defenses such as coughing.

Our study has several limitations. First, saline aerosols were used in place of actual bacterial or viral bioaerosols. This study was intended to look at airflow dynamics and hence use of a surrogate in the proper size range is sufficient to establish the possibility of migration into the ventilator tubes. Future work will focus on the use of aerosolized bacteria. Second, the test lungs used cannot match the complicated architecture and surface chemistry of actual lungs. A high propensity of adsorption to the interior surfaces of a lung would affect the concentration of material that can escape, however, we do not know to which degree immediate surface adsorption might occur between actual bioaerosols with an actual lung. Our study uses an experimental setup for convenience. This setup, although useful for the study presented herein, cannot simulate clinical conditions. We used low quantities of synthetic aerosols, however, we do not know the actual quantities generated during mechanical ventilation. The quantities of pathogenic aerosol generation are likely not constant. However, it is clear from our results that aerosolized material can enter the ventilator tubes on a short timescale. 48 hours or more of mechanical ventilation is considered the timeframe for developing VAP, which is considerably longer than the 10 s of exposure used in our study and gives considerable opportunity for aerosol migration and potentially colonization in the ventilator tubes. Our setup can be used with bioaerosols to study whether colonization can occur at specified sampling and aerosolization ports within the system.

Conclusion

We have demonstrated an experimental setup that allows for aerosols to be injected into a closed ventilator circuit and detected with a particle detector interfaced with the circuit. We have shown that small quantities of saline aerosols in the size range of 0.5-1.0 μm can be released at the endotracheal tube cuff region during mechanical ventilation at nozzle pressures of 10-13 hPa and detected with a particle collector connected to the distal ventilator tubing. The concentration of detected aerosols increases with nozzle pressure. Aerosols introduced below the endotracheal cuff can travel retrogradely into the ventilator tubing via the endotracheal tube. Mechanical ventilation does not prevent retrograde diffusion into the ventilator tubing. The experimental system described in this report is a model system that can help understand factors that might cause VAP and spur the introduction of technologies that might help prevent VAP. The setup can be further modified to study the potential for bioaerosol migration and contamination in ventilator tubes.

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